Citation:

Michaud DS, Fuchs CS, Liu S, Willett WC, Colditz GA, Giovannucci E. Dietary glycemic load, carbohydrate, sugar and colorectal cancer risk in men and women. *Cancer Epidemiol Biomarkers Prev*. 2005 Jan; 14 (1): 138-147.

PubMed ID: 15668487

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To determine the effect of quality and quantity of carbohydrates on colorectal cancer risk by examining the association between dietary carbohydrate, sucrose, fructose, glycemic index, glycemic load, and the risk of colon and rectal cancers in two large prospective cohorts.

Inclusion Criteria:

Participants of the Health Professionals Follow-up Study (initiated in 1986 with men aged 40-75 years) or the Nurses' Health Study (initiated in 1976 with female registered nurses aged 30-55 years).

Exclusion Criteria:

- Implausibly high or low caloric intake
- Those who reported a previous cancer diagnosis (other than nonmelanoma skin cancer)
- Ulcerative colitis
- Crohn's disease
- Familial polyposis syndrome at baseline.

Description of Study Protocol:

Recruitment

Study subjects were participants of two ongoing large cohort studies.

Design

Two prospective cohorts with repeated diet measures and up to 20 years of follow-up.

Dietary Intake/Dietary Assessment Methodology

Food-frequency questionnaires (FFQ).

Blinding Used

Not applicable.

Intervention

Not applicable.

Statistical Analysis

- Incidence rates of colorectal cancer were calculated by dividing the number of incident cases by the number of person-years in each category of dietary exposure. The relative risk (RR) for each of the upper categories was computed by dividing the rates in these categories by the rate in the lowest category
- Relative risks adjusted for potential confounders were estimated using Cox proportional hazards models stratified on age in years
- Tests for trend were conducted by assigning the median value to each category and modeling this variable as a continuous variable.

Data Collection Summary:

Timing of Measurements

- Nurses' Health Study: Diet was assessed with a FFQ in 1980, 1984, 1986 and every four years thereafter
- Health Professional Follow-Up Study: Diet was assessed with a FFQ in 1986, and every four years thereafter
- Changes in lifestyle habits and information on disease onset were obtained biennially since onset of the studies using mailed questionnaires
- Up to 20-year follow-up.

Dependent Variables

- Colorectal cancer
- Colon cancer
- Rectal cancer.

Participants were asked to report specified cancers that were diagnosed in the two-year period between each follow-up questionnaire. Confirmation was attempted with medical record review or additional questioning of the participant.

Independent Variables

- Dietary glycemic index
- Glycemic load
- Carbohydrate
- Sucrose
- Fructose were assessed using FFQ.

Control Variables

- Age
- Family history of colon cancer
- Prior endoscopy screening
- Aspirin use
- Height
- Body mass index
- Pack-years of smoking before age 30
- Physical activity
- Intakes of:
    - Cereal fiber
    - Alcohol
    - Calcium
    - Folate
    - Processed meat and beef
    - Pork
    - Lamb as a main dish.

Description of Actual Data Sample:

- *Initial N:* Nurses' Health Study: 121,700; Health Professionals Follow-up Study (original study cohort sizes)
- *Attrition (final N):* 131,349 (83,927 women and 47,422 men)
- *Age:*
    - Nurses' Health Study: 30-55 years
    - Health Professionals Follow-up Study: 40-75 years (at baseline)
- *Ethnicity:* Not reported
- *Other relevant demographics:* Not reported
- *Anthropometrics:* Body mass index did not vary appreciably across quintiles of glycemic load
- *Location:* US.

Summary of Results:

Key Findings

- High GL, and fructose and sucrose intakes were associated with increased colorectal cancer risk in men
- In women, these factors did not increase risk
- No associations were observed for dietary carbohydrate, glycemic load, glycemic index, sucrose, fructose and the risk of colorectal cancer in the Nurses' Health Study
- In the Health Professionals Follow-up Study, men with higher intakes of glycemic load (P for trend=0.04), sucrose (P for trend=0.03) or fructose (P for trend=0.008) had a slightly elevated risk of colorectal cancer
- Associations were slightly stronger among men with higher BMI (>25mg/kg^2).

Author Conclusion:

- Overall, study results suggest that glycemic response to diet may not play a major role in colorectal cancer
- There was a slight (27% to 37%) increase in the risk of colorectal cancer with increasing intakes of carbohydrate, glycemic load, sucrose or fructose in men, but no associations were observed in women.

Reviewer Comments:

- *Author-identified strengths: Prospective design, detailed information on diet and data on many potential risk factors of colorectal cancer*
- *Limitation: Height and weight were self-reported.*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes

2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	Yes
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	N/A
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	N/A
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	N/A
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A

5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	N/A
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes

8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	N/A
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	N/A
8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes